UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON D.C. 20460

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PREVENT ON, PEST C DES
AND TOX C SUBSTANCES

December 7, 1995

MEMORANDUM

Subject: EPA Reg. No.: 149-8 / Terro Ant Killer II

From: Ian Blackwell, Biologist IDB 12/7/95
Precautionary Review Section
Registration Support Branch
Registration Division (7505W)

To: Wanda Ruffin Daughtry
Planning and Reregistration Branch
Special Review and Reregistration Division (7508W)

Applicant: Senoret Chemical Company
566 Leffingwell Ave.
Kirkwood, MO 63122

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Sodium tetraborate decahydrate	5.4
Inert Ingredient(s):	94.6
Total:	100%

BACKGROUND: Senoret Chemical Company has submitted four acute oral toxicity studies, two acute dermal toxicity studies, three primary eye irritation studies, one primary skin irritation study and one dermal sensitization study in support of "Terro Ant Killer II". These studies were submitted in response to the Boric Acid RED. This product was placed into batch 17 of that RED. The MRID numbers are 436734-01, 436734-02, 423406-01, 423406-02, 1026-019-03, 2400-913-29 and 2402-045-09. MRID number 1026-019-03 and 2402-045-09 each contain an acute oral toxicity study, an acute dermal toxicity study and a primary eye irritation study.

The primary eye irritation (MRID number 423406-01) and skin irritation (423406-02) studies were previously reviewed by PRS on 8/19/93 and 4/25/95. A waiver request for the acute inhalation toxicity study was reviewed in a 7/14/95 PRS review of this product.

RECOMMENDATIONS:

1. Acute oral toxicity study (MRID) #436734-01 is classified as acceptable data and is sufficient to support the reregistration of the product.

2. The acute oral toxicity studies submitted in MRIDs 2402-045-09, 2400-913-29 and 1026-019-03 were not reviewed. The reasons are as follows:

   a. The test materials used were identified only as "TW-439", "CH 3565" and "TW-674". They were not identified by registration number, product name or CSF.
   b. The registrant had already submitted an acceptable acute oral toxicity study to support this product (MRID number #436734-01).
   c. MRID 2400-913-29 was conducted on mongrel dogs.
   d. None of these studies was conducted later than 1973. As each of these studies was conducted years before our current GLPs were developed. Such studies typically have several study inadequacies that prevent them from being acceptable.

3. Acute dermal toxicity study (MRID) number 2402-045-09 is classified as unacceptable data and is not suitable to support the registration of this or any product. This study cannot be upgraded and must be reconducted. The study deficiencies are as follows:

   a. The test material is not properly identified. The test material is only identified as "TW-439". The identification does not include a registration number, it does not give a product name, none of the ingredients are specified and the report does not even state whether the product is a solid or liquid.
   b. The lab did not test five males and five females at any of the dosages tested. The lab tested two animals per sex for most of the four dose levels tested. This flaw alone is sufficient reason for this study to not be accepted in support of any EPA registered product.
   c. The dimensions of the exposure site were not reported. This is another serious flaw.

d. The test material was introduced under paper that was attached to the animals' skin. The paper was then wrapped with gauze and adhesive tape. This may have caused excessive absorption of (what should have been) a liquid test material.
e. The test site was not wrapped with an occlusive material such as plastic wrap or a rubber dam. This can allow some of the test material to escape the gauze, which is supposed to act as a reservoir.
f. The test material was applied to the abdomen of the test animals. It is preferred that the test material be applied to the dorsum.
g. The report does not state how long a period of time passed between clipping the animals' fur and applying the test material.
h. Some of the test sites were abraded. The importance of this variation will depend on the study results.
i. The strain, age and source of the test animals were not reported.
i. The lab did not state compliance with GLP standards.
j. The lab did not certify having any type of Quality Assurance.
k. The report did not state how frequently clinical observations for illness or other abnormalities were made during the study.

4. Acute dermal toxicity study (MRID) number 1026-019-03 is classified as unacceptable data and is not adequate to support the registration of this or any other product. This study cannot be upgraded and must be replaced. The study deficiencies are as follows:

   a. The lab did not test five males and females per exposure level. This factor alone is sufficient cause for this study to not be accepted to support any product.
   b. The test material is not properly identified. The test material in this study is only identified as "TW-674". The report does not give a registration number, product name, give the chemical formulation nor does it even describe the test material. The registrant has not submitted information to link the test material to the registration product.
   c. The dimensions of the exposure area were not reported.
   d. The test material was applied to the test animals' abdomens.
   e. Some of the dose sites were abraded.
   f. The report did not state when, prior to test material administration, the animals were clipped.
   g. The age, strain and source of the test animals was not reported.
   h. The lab did not certify to compliance with GLP standards.
   i. No Quality Assurance was conducted.
   j. The report did not state how frequently the test animals were observed.

5. The acute inhalation toxicity study has been waived (see the 7/14/95 PRS review of this product). This product is assigned toxicity category IV for acute inhalation toxicity.

6. Primary eye irritation study (MRID) # 423406-01 is classified as acceptable data and is sufficient to support the reregistration of the product.

7. Primary eye irritation study #1026-019-03 is not currently acceptable to support the reregistration of this product. The problem with this study is that the test material is

identified as "TW-674". PRS does not know what TW-674 is. In order for this study to be reconsidered, the registrant must identify "TW-674" by:

a. the materials chemical formulation, or,
b. the test materials EPA registration number

PRS would like to point out that primary eye irritation study #423406-01 has been accepted to support this product and has been categorized as toxicity category IV. PRS has not attempted to review MRID #1026-019-03 and it is very likely that this study has several flaws as did dermal toxicity study #1026-019-03. The registrant needn't submit additional information to support MRID #423406-01 unless they are trying to move the toxicity category of this product from IV to **III**.

8. Primary skin irritation study (MRID) # 423406-02 is classified as acceptable data and is sufficient to support the reregistration of the test material.

9. Dermal sensitization study (MRID) #423406-03 is classified as supplementary data, but may be upgraded. In order for this study to be reconsidered, the registrant must submit a positive control study conducted by MB Research Laboratories within a six month period of the main dermal sensitization study. Otherwise, the registrant will have to submit another dermal sensitization study to support this product.

The acute toxicity profile for reg. no. 149-8 is currently:

acute oral toxicity	IV	acceptable
acute dermal toxicity		unacceptable
acute inhalation toxicity	IV	(WAIVED)
primary eye irritation	IV	acceptable
primary skin irritation	IV	acceptable
dermal sensitization		supplementary

LABELING:

As three of the six acute toxicity/ irritation studies required to support this product are not acceptable or have not been submitted, PRS cannot recommend precautionary labeling for this product at this time.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1)

Product Manager: 10
MRID No.: 436734-01

Reviewer: I. Blackwell
Study Completion Date: 9/26/94
Report No.: MB 94-3943

Testing Facility : MB Research Laboratories, Inc.
Authors : Daniel R. Cerven

Quality Assurance (40 CFR §160.12): Included

Test Material: Terro ant Killer II

Species: Wistar albino rats
Age: 9-11 weeks (approx.)
Weight: males = 225-240 g; females = 218-225 g
Source: Ace Animals

Conclusion:

1. **LD_{50} (mg/kg):** **Males** > 5000 mg/kg
Females > 5000 mg/kg
Combined > 5000 mg/kg
2. **The estimated LD_{50} is greater than 5000 mg/kg of body weight.**
3. **Tox. Category:** IV **Classification**: acceptable

Procedure (Deviations from §81-1):

Results:

Dosage (mg/kg)	(Number Killed/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: Anogenital wetness and soiling; diarrhea.

Gross Necropsy: Slight or scattered hydronephrotic kidneys and moderate or few hard white masses in urinary bladder.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: 10
MRID No.: 2402-045-09

Reviewer: Ian Blackwell
Report Date: 2/21/69
Report No.: T-24A

Testing Laboratory: Hill Top Research, Inc.
Author: Richard H. Teske, DVM

Quality Assurance (40 CFR §160.12): not included

Test Material: TW-439

Species: albino rabbit
Weight: 2002-2922 grams
Age: not specified
Source: not specified

Summary:

1. **LD_{50} (mg/kg)**: **Males =**
   Females =
   Combined =

2. **The estimated LD_{50} is**

3. **Tox. Category**: **Classification**: unacceptable

Procedure (Deviation From §81-2):
*The test material is not properly identified.
*The lab did not test five males and five females per dose level.
*The dimensions of the exposure site were not reported.
*The test material was introduced under paper and then wrapped with gauze and adhesive tape.
*The exposure site was not wrapped with an occlusive material (e.g. plastic wrap).
*The test material was applied to the abdomen of the animals.
*The report did not state how soon before the exposure that the animals were clipped.
*Some of the test sites were abraded.
*Strain, age and source of the test animals not specified.
*Lab did not state that study met GLP requirements.
*The lab did not certify to any form of Quality Assurance.
*The report did not state when or how frequently observations were made.

Results:

Reported Mortality

DOSAGE	(NUMBER KILLED/NUMBER TESTED)		
	Males	**Females**	**Combined**
1.00 g/kg	0/2	0/2	0/4
2.15 g/kg	0/1	0/3	0/4
4.64 g/kg	0/2	0/2	0/4
10.0 g/kg	0/2	0/2	0/4

Observations: Mild or moderate erythema, edema ataxia and depression, diarrhea.

Gross Necropsy Findings: No significant pathological alterations.

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: 10
MRID No.: 1026-019-03

Reviewer: Ian Blackwell
Report Date: 1/15/73
Report No.: 72-506-21(1)

Testing Laboratory: Hill Top Research, Inc.
Author: Paul A. Majors

Quality Assurance (40 CFR §160.12): not included

Test Material: TW-674

Species: albino rabbits
Weight: 2325-2980 grams
Age: not specified
Source: not specified

Summary:

1. **LD_{50} (mg/kg)**: **Males =**
   Females =
   Combined =

2. **The estimated LD_{50} is**

3. **Tox. Category**: **Classification**: UNACCEPTABLE

Procedure (Deviation From §81-2):
*The lab did not test five males and five females per exposure level.
*The test material is not properly identified.
*The test site was covered with freezer wrapper paper and then with gauze.
*The dimensions of the exposure area were not reported.
*The test material was applied to the animals' abdomens..
*Some of the dose sites were abraded.
*The report did not state how long before exposure the animals' fur was clipped.
*The age, strain and source of the test animals were not identified.
*The lab did not certify to GLP standards.
*No quality assurance was conducted.
*The report did not state how frequently the test animals were observed.

Reported Mortality

DOSAGE	(NUMBER KILLED/NUMBER TESTED)		
	Males	**Females**	**Combined**
1.00	0/2	0/2	0/4
2.15	0/3	0/1	0/4
4.64	0/2	0/2	0/4
10.0	2/3	0/1	2/3

Observations: Erythema, edema, blanching, necrosis, sloughing

Gross Necropsy Findings: Congested lungs and kidneys, depleted body-fat stores, irritation of intestines, diffuse dark areas on liver, adhesions between liver and peritoneum and diaphragm, abscess-like bodies adherent to urinary bladder and peritoneum.

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DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6)

Product Manager: 10
MRID No.: 436734-02

Reviewer: I. Blackwell
Study Completion Date: 10/17/94
Report No.: MB 94-3943 F

Testing Laboratory: MB Research Laboratories, Inc.
Author: Theresa Newcomb

Quality Assurance (40 CFR §160.12): Included

Test Material: Terro Ant Killer II #3684-B; "clear liquid"
Positive Control Material: not specified

Species: Hartley albino guinea pigs
Weight: 306-367 g
Age: not specified
Source: Ace Animals

Method: Buehler Method

Summary:

1. **This Product is / is not a dermal sensitizer.**

2. **Classification**: supplementary

Procedure (Deviation From §81-6):
*No positive control data was included in this report.
*The quality assurance statement was signed by the Study Director.

Results: The test material was screened at 100, 50, 25 and 10% concentrations. The test animals were induced with 0.4 ml of 100% test material once a week for three weeks. The test material was applied for six hours for each induction. Challenge was conducted in the same manner.

No irritation was observed after any of the three induction treatments. No irritation was observed after challenge with the test material. No irritation was observed in any of the naive control animals following challenge.

ACUTE TOX ONE-LINER

1. PC CODE: 011102

2. CURRENT DATE: December 5, 1995

3. TEST MATERIAL: sodium tetraborate decahydrate ... 5.4%

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade
acute oral toxicity / rat / MB Research Laboratories, Inc. / MB 94-3943 / 9-26-94	436734-01	LD_{50} > 5000 mg/kg for both sexes	IV	A
acute dermal toxicity / rabbit / Hill Top Research, Inc. / T-24A / 2-21-69	240204509			U
acute dermal toxicity / rabbit / Hill Top Research / 72-50621C / 1-15-73	102601903			U
dermal sensitization / guinea pig / MB Research Laboratories / MB 94-3943F / 10-17-94	436734-02			S

Core Grade Key:

A = Acceptable
U = Unacceptable
S = Supplementary (upgradeable)